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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF PREVENTION,
PESTICIDES AND TOXIC
SUBSTANCES

APR 0 [illegible] 2003

MEMORANDUM

SUBJECT: BPPD Review of Acute Pulmonary and Pathogenicity to the Rat, and Hypersensitivity Incidents - Human Data Submitted by Arizona Cotton Research and Protection Council for *Aspergillus flavus* F36 (Submission No.: S624885; DP Barcode: 286705; MRID No's.: 457981-01, 457391-01, 457982-01, and 457391-04).

TO: Shanaz Bacchus (PM-90), Regulatory Action Leader
Microbial Pesticides Branch, Biopesticides and
Pollution Prevention Division (7511C)

FROM: Carl Etsitty, M.S., Microbiologist
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THROUGH: John L. Kough, PH.D., Senior Scientist
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ACTION REQUESTED: Review the submitted data for acute pulmonary and pathogenicity to the rat, and hypersensitivity incidents - human, to determine the adequacy in support *Aspergillus flavus* atoxigenic strain AF36 for use on cotton to displace the toxigenic strain.

BACKGROUND: Arizona Cotton Research and Protection Council submitted data on acute pulmonary toxicity and pathogenicity to the rat, and human hypersensitivity incidents to support their application for a registration for *Aspergillus flavus* AF36 (active ingredient), an atoxigenic fungal competitor to displace the toxigenic strain.

One of these studies is in response to the previously submitted data which indicated a number of adverse effects (deaths) in the test animals. The first data generated covered a preliminary study which were included and reported elsewhere; yet, not repeated in MRID 45739-01. Secondly, MRID 457391-01 includes "Comments on Use of Tween 80 in Protocol UAR/004" and gives an explanation of toxicity observed in UAR/004 (MRID 457981-01) attributed to use of Tween 80 in the vehicle. It also includes a number of Tween 80 literature citations confirming the attributed toxicity. Thirdly, MRID 457391-01 in the same submission includes "Comments on Use of Tween 80 in Protocol UAR/004" and gives the explanation that toxicity observed is attributable to using Tween 80 as the vehicle, and MRID 457982-01 in the same submission includes a similar study using the same test organism without using Tween 80 as the vehicle. Lastly, the registrant is reminded that it's the registrant responsibility to report any adverse reaction

Aspergillus flavus AF36 is labeled for outdoor use, and on cotton only to displace toxigenic *Aspergillus flavus* strains. The usage rates: 10lbs of AF36 per acre (per 13,000 linear feet based on 40 inch rows).

CONCLUSION: No inhalation data was provided to conclude an adequate toxicity classification; however based on MRID 457981-01, TOXICITY Category III for no foreseeable effect for inhalation data.

DATA REVIEW RECORD

Active Ingredient:	*Aspergillus flavus* Strain AF36	
Product Name:	None given	
Company Name:	Arizona Cotton Research and Protection Council	
ID No:	071693-R *Aspergillus flavus* AF36	
Chemical No.:	006456 *Aspergillus flavus* 36 colonized wheat seed	
Submission No.:	S624885	
DP Barcode:	286705	
MRID No:	457391-01	Acute Pulmonary Toxicity/Pathogenicity - Rats
	457391-04	Hypersensitivity Incidents
	457981-01	Acute Pulmonary Toxicity/Pathogenicity - Rats
	457982-01	Acute Pulmonary Toxicity/Pathogenicity - Rats

SUMMARY OF DATA SUBMITTED:

457391-01:Acute Pulmonary Toxicity/Pathogenicity - Rats (OPPTS 885.3150)

This study was a preliminary study to investigate a suitable concentration of *Aspergillus flavus* AF36 to be used in a main study for an acute pulmonary toxicity and pathogenicity to the rat. This study concluded that 10^8 cfu/rat would be a suitable dose level.

CLASSIFICATION: Supplemental data to support further studies.

457391-04: Hypersensitivity Incidents (OPPTS 885.3400)

No recorded or reported adverse hypersensitivity reaction to the *Aspergillus flavus* AF36 was reported by one state council and six companies during use for 3 or 6 years.

CLASSIFICATION: ACCEPTABLE

457981-01: Acute Pulmonary Toxicity/Pathogenicity - Rats (OPPTS 885.3150)

Aspergillus flavus AF36 appears to have initial dosing effect resulting in 14 deaths by day 4, but was not infective or pathogenic, with clearance by day 8, when dosed with 1.2 mL/kg at 5.30×10^8 cfu/mL (or $1.28\text{-}1.63 \times 10^8$ cfu/animal) to the test animals.

CERTIFICATION: ACCEPTABLE

457982-01: Acute Pulmonary Toxicity/Pathogenicity - Rats (OPPTS 885.3150)

Aspergillus flavus AF36 appears to have initial dosing effect resulting in 1 female and 3 male rat deaths on day 2. The rest of test animals showed an initial response but rapid recovery indicating no toxicity, and that AF36 was non-infective, and/or pathogenic to rats when dosed at $1.93\text{-}2.90 \times 10^8$ cfu/rat, with observable clearance patterns.

CERTIFICATION: ACCEPTABLE

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R141573

Chemical: Aspergillus flavus 36 colonized wheat seed

PC Code:
006456

HED File Code: 41500 BPPD Tox/Chem
Memo Date: 4/2/2003
File ID: DPD286705
Accession #: 000-00-9002

HED Records Reference Center
4/13/2007